

CLAIMS:

1. A method for reducing the occurrence of fever, headache, nausea and/or vomiting associated with administration of a therapeutic compound to a mammal in need thereof, comprising:
5 administering to the mammal a first conditioning dose of a non-target cell-depleting compound which binds to a cell surface receptor on a target mammalian cell; and
administering a second therapeutic dose of the compound, wherein the second dose is higher than the first dose.
- 10 2. The method of claim 1, wherein the therapeutic compound comprises a polypeptide which binds to an extracellular domain of the receptor molecule.
3. The method of claim 2, wherein the polypeptide is an antibody or a fragment thereof.
- 15 4. The method of claim 1, wherein the target mammalian cell is a lymphocyte.
5. The method of claim 4, wherein the lymphocyte is a T-cell.
6. The method of claim 5, wherein the cell surface receptor on the T cell is LFA-1.
- 20 7. The method of claim 6, wherein the therapeutic compound is anti-CD11a antibody hu1124.
8. The method of claim 1, further comprising administering a third therapeutic dose, wherein the third dose is higher than the second dose.
- 25 9. The method of claim 1, wherein administration is intravenous or subcutaneous.
10. The method of claim 1, wherein administration is not more than once per week.
- 30 11. A method for treating an LFA-1 mediated disorder, comprising
administering to a mammal in need thereof a first conditioning dose of a compound which binds to the lymphocyte surface receptor LFA-1; and
administering a second therapeutic dose of the compound, wherein the second dose is higher than the first dose.
- 35 12. The method of claim 11, wherein the compound comprises a polypeptide which binds to an extracellular domain of the receptor molecule.
13. The method of claim 12, wherein the polypeptide is an antibody or a fragment thereof.
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14. The method of claim 13, wherein the antibody or fragment thereof binds to CD11a.
15. The method of claim 14, wherein the antibody is antibody hu1124.
- 5 16. The method of any one of claims 11-15, wherein the LFA-1 mediated disorder is selected from the group consisting of psoriasis, asthma, rheumatoid arthritis, multiple sclerosis, rejection of a transplanted graft or rejection by a transplanted graft.
17. The method of claim 16, wherein the transplant is a renal transplant.
- 10 18. The method of claim 11, further comprising administering a third therapeutic dose, wherein the third dose is higher than the second dose.
19. The method of claim 11, further comprising administering a fourth therapeutic dose, wherein the fourth
15 dose is higher than or equal to the third dose.
20. The method of claim 11, wherein administration is intravenous or subcutaneous.
21. The method of claim 11, wherein administration is not more than once per week.
- 20 22. The method of claim 11, wherein the compound is non-lymphocyte depleting.
23. A method for conditioning a mammal to tolerate high doses of a therapeutic compound, comprising
administering to the mammal a first conditioning dose of a non-target cell depleting compound which
25 binds to a cell surface receptor on a target mammalian cell ; and
administering a second therapeutic dose of the compound, wherein the second dose is higher than the
first dose.
24. A method for down modulating a cell surface receptor in a cell population in a mammal, comprising
30 contacting a target mammalian cell displaying a receptor molecule on the surface thereof with a first
dose of a ligand which binds to the receptor molecule and does not deplete the target mammalian cell
population; and then
further contacting the target mammalian cell population with a second dose of the ligand, wherein the
second dose is higher than the first dose.
- 35 25. The method of claim 24, wherein the ligand comprises a polypeptide which binds to an extracellular
domain of the receptor molecule.
26. The method of claim 25, wherein the polypeptide is an antibody or a fragment thereof.
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27. The method of any one of claims 24-26, wherein the target mammalian cell is a lymphocyte.
- 5 28. The method of claim 27, wherein the lymphocyte is a T-cell.
29. The method of claim 28, wherein the cell surface receptor is CD11a and the ligand is antibody hu1124.
30. The method of claim 24, further comprising contacting the mammalian cell population with a third
10 dose of the ligand, wherein the third dose is higher than the second dose.
31. The method of claim 24, wherein the contacting is by administration to a mammal.
32. The method of claim 31, wherein administration is not more than once per week.
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